

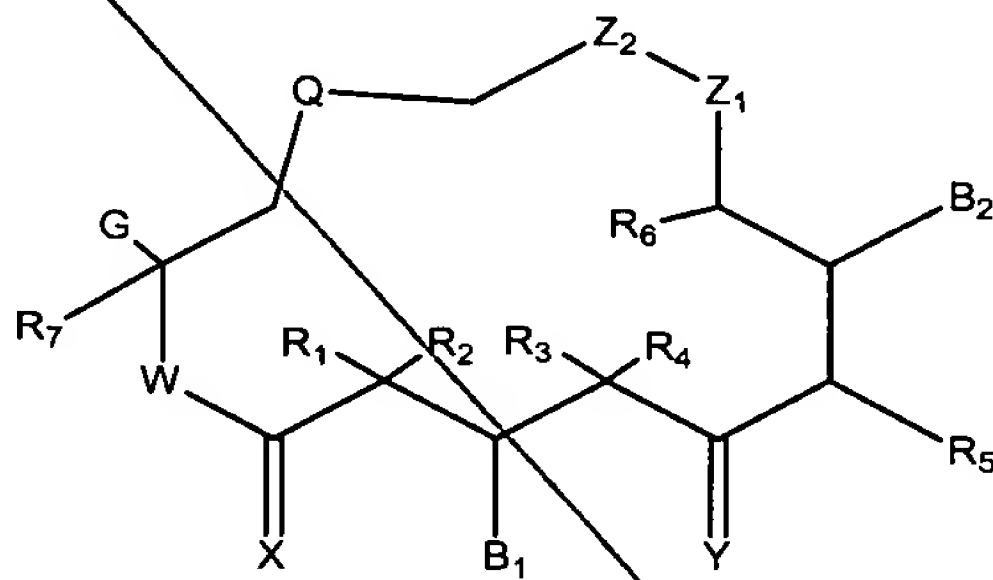
- hematopoietic tumors of myeloid lineage, including acute and chronic myelogenous leukemias and promyelocytic leukemia;--
- tumors of the central and peripheral nervous system, including astrocytoma, neuroblastoma, glioma, and schwannomas;
- tumors of mesenchymal origin, including fibrosarcoma, rhabdomyosarcoma, and osteosarcoma; and
- other tumors including melanoma, xenoderma, pigmentosum, keratoactanthoma, seminoma, thyroid follicular cancer and teratocarcinoma.--

IN THE CLAIMS

A marked up version of the amended claims showing insertions and deletions is attached hereto as Exhibit B. For the Examiner's convenience a list of the currently pending claims is attached hereto as Exhibit C.

Please cancel claims 5-6, 9-10, and 12-13 and rewrite claims 1, 4, 7-8, 11, and 14 as follows:

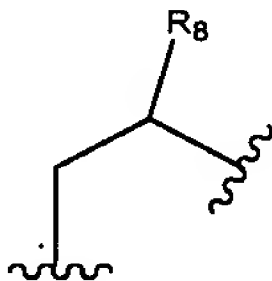
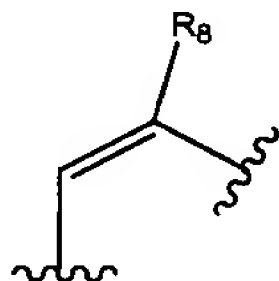
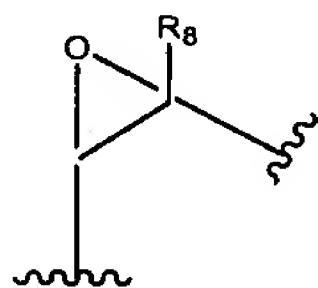
1. (Thrice amended) A compound of the formula



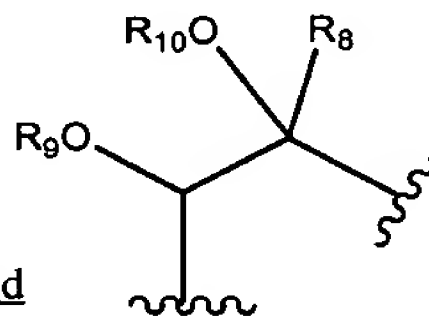
V

wherein

Q is selected from the group consisting of

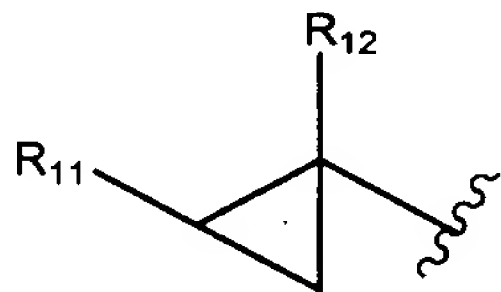
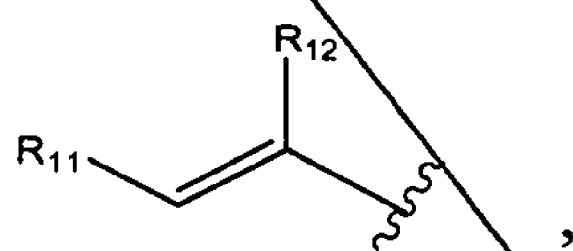


and

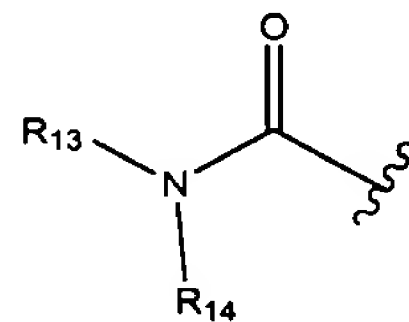


E 2
cont

G is selected from the group consisting of alkyl; substituted alkyl; substituted aryl; a 4 to 7 membered monocyclic, 7 to 11 membered bicyclic, or 10 to 15 membered tricyclic ring system having between 1 and 3 heteroatoms selected from nitrogen, oxygen, and sulfur;



and



W is O or NR₁₅;

X is O or H, H;

Y is selected from the group consisting of O; H, OR₁₆; OR₁₇, OR₁₇; NOR₁₈; H, NOR₁₉; H, NR₂₀R₂₁; H, H; and CHR₂₂; wherein OR₁₇, OR₁₇ can be a cyclic ketal;

Z₁ and Z₂ are independently CH₂;

D 2

B₁ and B₂ are independently selected from the group consisting of OR₂₄, OCOR₂₅, and O-C(=O)-NR₂₆R₂₇, and when B₁ is H and Y is OH, H, they can form a six-membered ring ketal or acetal;

R₁, R₂, R₃, R₄, R₅, R₇, R₁₃, R₁₄, R₁₈, R₁₉, R₂₀, R₂₁, R₂₂, R₂₆ and R₂₇ are selected from the group consisting of H, alkyl, substituted alkyl, and aryl, and when R₁ and R₂ are alkyl can be joined to form a cycloalkyl, and when R₃ and R₄ are alkyl can be joined to form a cycloalkyl;

R₆ is methyl;

R₉, R₁₀, R₁₆, R₁₇, R₂₄, R₂₅ and R₃₁ are selected from the group consisting of H, alkyl, and substituted alkyl;

R₁₁, R₁₂, R₂₈, R₃₀, R₃₂, and R₃₃ are selected from the group consisting of H, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl and heterocyclo;

R₈ is hydrogen or methyl;

R₁₅, R₂₃ and R₂₉ are selected from the group consisting of H, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, heterocyclo, R₃₂C=O, R₃₃SO₂, hydroxy, O-alkyl or O-substituted alkyl; and

the pharmaceutically acceptable salts thereof and any hydrates, solvates or geometric, optical and stereoisomers thereof;

with the proviso that compounds wherein

W and X are both O; and

D2
E2
Cont
R₁, R₂ and R₇ are H; and

R₃, R₄ and R₆ are methyl; and

R₈ is H or methyl; and

G is 1-methyl-2-(substituted-4-thiazolyl)ethenyl; and

Q is as defined above

are excluded.

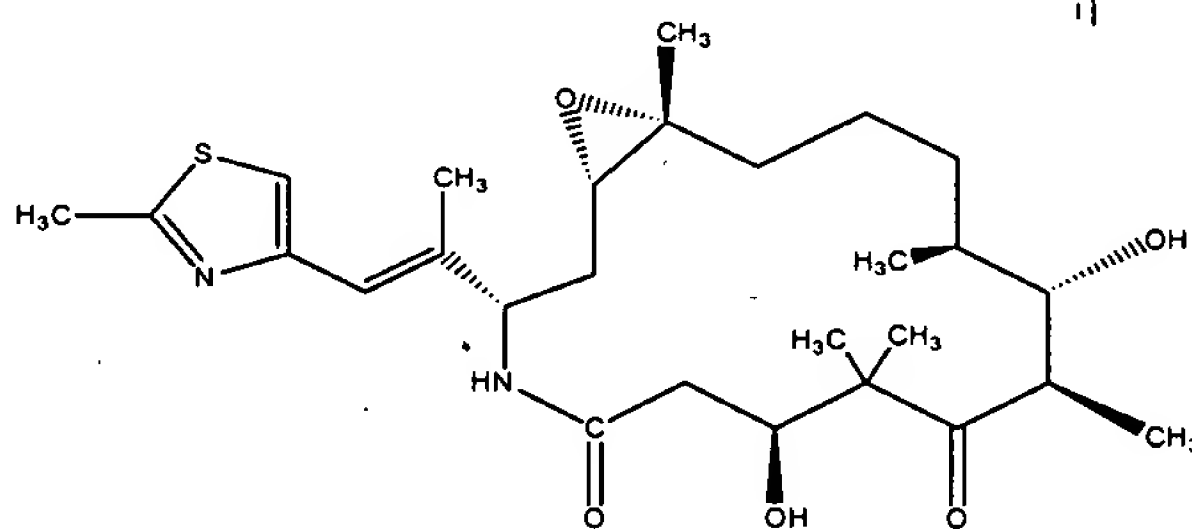
D3
para
E3
4. (Thrice amended) A method of treating breast cancer, ovary cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 1.

5 *7* (Amended) The method of claim 4, wherein the cancer is cancer of the breast, ovary, or colon.

D4
para
E4
8. (Amended) A method of treating breast cancer, ovary cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 2.

D5
para
E5
11. (Amended) A method of treating breast cancer, ovary cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 3.

para D6
E6
14. (Amended) The compound of claim 1 having the formula:



or a pharmaceutically acceptable salt, hydrate, solvate, geometrical isomer, optical isomer, or stereoisomer thereof.

Please add the following new claims:

15. (New) A method of treating breast cancer, ovary cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 14.

16. (New) The method of claim 15, wherein the cancer is cancer of the breast, ovary, or colon.

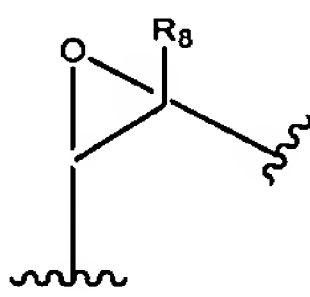
17. (New) The method of claim 8, wherein the cancer is cancer of the breast, ovary, or colon.

18. (New) The method of claim 11, wherein the cancer is cancer of the breast, ovary, or colon.

19. (New) The compound of claim 1, wherein G is 1-methyl-2-(substituted-4-thiazolyl) ethenyl group.

20. (New) The compound of claim 1, wherein Q is

7,0730



¹⁵ 21. (New) The compound of claim 1, wherein W is NR₁₅.

¹⁶ 22. (New) The compound of claim 1, wherein X and Y are each O.

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E7

23. (New) A method of treating breast cancer, ovary cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 19.

¹⁸ 24. (New) The method of claim ¹⁷23, wherein the cancer is cancer of the breast, ovary, or colon.

P
E8

25. (New) A method of treating breast cancer, ovary cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 20.

²⁰ 26. (New) The method of claim ¹⁹25, wherein the cancer is cancer of the breast, ovary, or colon.

P
E9

27. (New) A method of treating breast cancer, ovary cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in

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cont
need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 21.

22 28. (New) The method of claim 27, wherein the cancer is cancer of the breast, ovary, or colon.

21
29. (New) A method of treating breast cancer, ovary cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 22.

24 30. (New) The method of claim 29, wherein the cancer is cancer of the breast, ovary, or colon.

25 31. (New) A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 1.

26 32. (New) A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 2.

27 33. (New) A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 3.

28 34. (New) A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 14. 8

29 35. (New) A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 19.¹³

30 36. (New) A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 20.¹⁴

07 31 37. (New) A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 21.¹⁵

32 38. (New) A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 22.¹⁶

33 39. (New) The method of claim 4, further comprising administering one or more of a additional anti-cancer agent.

34 40. (New) The method of claim 39,³³ wherein the additional anti-cancer agent acts in a phase of the cell cycle other than the G₂-M phase.

35 41. (New) The method of claim 40,³⁴ wherein the additional anti-cancer is a thymidilate synthase inhibitor, a DNA cross linking agent, a topoisomerase I or II inhibitor, a DNA alkylating agent, a ribonuclease reductase inhibitor, a cytotoxic factor, or a growth factor inhibitor.

36 42. (New) The method of claim 4, further comprising administering radiation therapy.

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37 43. (New) A pharmaceutical composition comprising the compound of claim 1 and a pharmaceutically acceptable vehicle or diluent.

38 44. (New) A pharmaceutical composition comprising the compound of claim 2 and a pharmaceutically acceptable vehicle or diluent.

39 45. (New) A pharmaceutical composition comprising the compound of claim 3 and a pharmaceutically acceptable vehicle or diluent.

07 40 46. (New) A pharmaceutical composition comprising the compound of claim 14⁸ and a pharmaceutically acceptable vehicle or diluent.

41 47. (New) A pharmaceutical composition comprising the compound of claim 19¹³ and a pharmaceutically acceptable vehicle or diluent.

42 48. (New) A pharmaceutical composition comprising the compound of claim 20¹⁴ and a pharmaceutically acceptable vehicle or diluent.

43 49. (New) A pharmaceutical composition comprising the compound of claim 21¹⁵ and a pharmaceutically acceptable vehicle or diluent.

44 50. (New) A pharmaceutical composition comprising the compound of claim 22¹⁶ and a pharmaceutically acceptable vehicle or diluent.

45 51. (New) A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Kaposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 1.

46 52. (New) A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Kaposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 2.

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D

47 53. (New) A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Kaposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 3.

48 54. (New) A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Kaposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 14.⁸

07 49 55. (New) A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Kaposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 19.¹³

50 56. (New) A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Kaposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 20.¹⁴

51 57. (New) A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Kaposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 21.¹⁵

52 58. (New) A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Kaposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 22.¹⁶
